Claim 1 was rejected under the first paragraph of 35 U.S.C. §112. In the Advisory Action, the Examiner found Applicants' arguments unconvincing "because the limitation '60 % identity' along with 'differentially or preferentially expressed' could include many other unrelated genes".

The Examiner appears to have overlooked, however, that claim 1 requires that the sequences which claimed in addition to SEQ ID NO:1 and SEQ ID NO:3 must have the defined degree of similarity to those specified sequences ***and be hybridizable to those sequences under high stringency conditions*** and meet the recited functional criterion.

The PTO has provided guidelines for applying the written description requirement to biotechnology applications. Example 9 in those guidelines deals with hybridization. In guideline Example 9, the claim in question is drawn to a genus of nucleic acids all of which must hybridize with SEQ ID NO:1 and must encode a protein with a specific activity. Highly stringent hybridization conditions (6xSSC and 65 degrees Celsius) are disclosed. The application in the guidelines discloses only one species (SEQ ID NO:1 itself) falling within the scope of the claimed genus. The analysis provided by the guidelines is as follows:

> ... a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs. Thus, a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention.

Similarly, in the present application, the claim in question is drawn to a genus of nucleic acids all of which must hybridize under stringent conditions with a

specified sequence and all of which have a recited useful property (expressing differential amounts of mRNA in a normal vs. diseased state of a subject, which difference is detectable.). The nucleic acids claimed here are even further described as -- in addition to the two factors paralleling those in the guidelines -- having at least about 60% similarity to the full length of the specified sequences.

In determining whether an isolated nucleic acid falls within the scope of claim 1, a person skilled in the art would first determine whether the nucleic acid in question had at least about 60% similarity to SEQ ID NO:1 or to SEQ ID NO:3. Assuming the nucleic acid in question passed that test, the person skilled in the art would then determine ***whether it hybridizes to SEQ ID NO:1 or to SEQ ID NO:3 under the stringent conditions recited*** in claim 1. In fact, the stringency recited in claim 1 (0.1xSSC, 65°C) is even higher than the conditions in guideline Example 9 (6xSSC, 65°C), due to the lower salt concentration recited in claim 1 herein. If the nucleic acid in question were found to pass this second test too, it would necessarily have a great deal in common structurally with SEQ ID NO:1 or SEQ ID NO:3, and its expression profile would likely parallel those of the reference sequence. The specification herein -- see e.g. paragraphs [0114] and [0115] -- provides ample exemplification of how to determine whether a nucleic acid meets the requirements set forth in claim 1.

Clearly, the rejection of record under the first paragraph of 35 U.S.C. §112 cannot be sustained, and its withdrawal is respectfully solicited.

Claim 18 was rejected under the first paragraph of 35 U.S.C. §112, the Examiner arguing that the specification at paragraph [0080] does not communicate that the specific fragment recited in claim 18 is Applicants'

invention. The specification contains a description of each and every nucleotide in SEQ ID NO:1. Claim 18 simply recites some but not all of those expressly disclosed nucleotides. Therefore there is no basis for the contention that the specification does not convey that Applicants had possession of the expressly disclosed nucleotides contemplated by claim 18.

It is respectfully requested that this application be passed to issue with claims 1 and 15-18. If the Examiner has any questions concerning this application, the Examiner is requested to contact Richard Gallagher, Reg. No. 28,781, at (703) 205-8008.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a two (2) month extension of time for filing a reply in connection with the present application, and the required fee of $205.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,
BIRCH, STEWART, KOLASCH & BIRCH, LLP

By _____
Mark J. Nuell (Reg. No. 36,623)
P. O. Box 747
Falls Church, VA 22040-0747
(703) 205-8000

DRN/RG